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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GOON, SCARLETT Y	
ART UNIT	PAPER NUMBER
4131	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/540,619	KAJIHARA ET AL.	
	Examiner	Art Unit	
	SCARLETT GOON	4131	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24* is/are rejected.

7)☒ Claim(s) *11,13 and 14* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *24 June 2005, 15 December 2005, 17 April 2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is a National Stage entry of PCT/JP03/16682 filed on 25 December 2003 and claims priority to Japan foreign application 2002-377819 filed on 26 December 2002. A certified copy of the foreign priority document in Japanese has been received. No English translation has been received.

The preliminary amendment filed on 24 June 2005 in which claims 1-4 and 6-14 were amended, is acknowledged.

Claims 1-14 are pending in the instant application.

Information Disclosure Statement

The information disclosure statement (IDS) dated 24 June 2005, 15 December 2005 and 17 April 2008 complies with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609. Accordingly, they have been placed in the application file and the information therein has been considered as to the merits.

Claim Objections

Claims 11 and 13-14 are objected to because of the following informalities: The descriptive word used for a biotin-modified compound should be "biotinylated," not "biotinated". Appropriate correction is required.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by

multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).
A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.
Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 1 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 18 of U.S. Patent No. 7,135,566 B2 in view of published research article by Shao *et al.* and Calbiochem's immobilized immunochemical "Avidin-Agarose," catalog no. 189742 (2000-2001 General Catalog).

Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the patent are drawn to an asparagine-linked oligosaccharide of the formula shown in claim 18 wherein R^3 and R^4 are each a hydrogen atom or a group selected from the structures shown in said claim.

The claim of the instant application is drawn to an asparagine-linked oligosaccharide of formula (1) wherein R^1 and R^2 are each a hydrogen atom or a group selected from the formula (2) to (6), and Q is a biotin group or a FITC group.

The patent does not expressly disclose the modification of the structure in claim 18 with a biotin group. However, Shao *et al.* discloses a method for the preparation of asparagine-linked glycans derivatized with biotin to form the biotinyl-Asn or [6-(biotinamido)hexanoyl]-Asn derivative (p. 78 under subheading "preparation of biotinylglycans"). The biotinylglycans are shown in figure 1 (p. 78).

The "Avidin-Agarose" immobilized immunochemical of Calbiochem is an avidin-based matrix for chromatography of biotinylated proteins, peptides and ligands.

One of ordinary skill in the art would have been motivated to use the method described by Shao *et al.* to derivatize the oligosaccharides of claim 18 of U.S. Patent No. 7,135,566 B2 with a biotin group. As suggested by Calbiochem, their "Avidin-Agarose" product can be used to bind biotinylated glycans. A skilled artisan is aware that immobilized biotinylglycans can be used to purify proteins, such as antibodies, for pharmaceutical purposes, and this would result in a homogenous product. One of ordinary skill in the art would appreciate obtaining a homogenous product when the proteins are used for pharmaceutical purposes since it is well-known that impurities can lead to protein instability and deleterious side effects if formulated into a pharmaceutical composition.

Thus, instant claim 1 is seen to be obvious over claim 18 of U.S. Patent No. 7,135,566 B2 in view of published research article by Shao *et al.*

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 11 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Shao *et al.* (Anal. Biochem. 1992).

Shao *et al.* discloses a method for characterizing lectin specificity using streptavidin-biotinylglycans. Twelve asparagine-linked glycans of the high-mannose, hybrid, and complex type were derivatized with biotin to form the biotinyl-Asn or [6-(biotinamido)hexanoyl]-Asn derivative (p. 78 under subheading "preparation of biotinylglycans"). The biotinylglycans are shown in figure 1 (p. 78). The structures of particular relevance are the sialylated structures which include a decasaccharide (structure 11) and an undecasaccharide (structure 12), of the formula $SiaGal_2GlcNAc_2Man_3$-R and $Sia_2Gal_2GlcNAc_2Man_3$-R, respectively, where R is $GlcNAc_2$-[6-(biotinamido)hexanoyl]-Asn. The sialic acid residue of these structures is linked to galactose via an $\alpha(2,3)$-linkage. To assay the oligosaccharide-binding specificity of a panel of lectins, the lectins are linked to horseradish peroxidase (HRP) and streptavidin is applied to each well of a micotiter plate, followed by the addition of a selected biotinylglycan solution (p. 78-79 under subheading "the assay of oligosaccharide-binding specificity of the lectins"). After immobilization of the biotinylated asparagine-linked oligosaccharide to the microtiter plate, the lectins are assayed for oligosaccharide-binding specificity by measuring the release of chromagen from lectin–HRP binding to the immobilized oligosaccharide.

The sialylated biotinylglycans and microtiter assay developed to test for oligosaccharide specificity of various lectins, disclosed by Shao *et al.*, anticipates claims 1-2, 11 and 13.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Section [0001]

Claims 3-10 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shao *et al.* (Anal. Biochem. 1992) as applied to claims 1-2, 11 and 13 above, and further in view of Lin *et al.* (Bioorg. & Med. Chem. 1995), Bundy *et al.* (Anal. Chem. 2001) and Calbiochem's immobilized immunochemical "Avidin-Agarose," catalog no. 189742 (2000-2001 General Catalog).

The teachings of Shao *et al.* were as described above in the claim rejections under 35 USC § 102. Shao *et al.* does not teach an asparagine-linked oligosaccharide of formula (1) wherein R^1 is the group of formula (2) and R^2 is the group of formula (3), nor does it teach an asparagine-linked oligosaccharide of formula (1) wherein R^1 is the group of formula (3) and R^2 is the group of formula (2). Additionally, Shao *et al.* does not teach an asparagine-linked oligosaccharide derivative, that is modified with a biotin group, containing at least one fucose attached to N-acetylglucosamine on the nonreducing terminal side of the asparagine-linked oligosaccharide. Furthermore, Shao *et al.* does not teach an affinity column having immobilized thereto a biotinylated asparagine-linked oligosaccharide of formula (1).

Lin *et al.* teaches the enzymatic synthesis of a dimeric sialyl Lewis x (sLe^x) glycopeptide from an N-linked oligosaccharide prepared from egg yolk. The structure for the dimeric sLe^x glycopeptides is shown in figure 3(a). The method for the preparation of the structure is described in the experimental section (p. 1627) and shown in figure 4 (p. 1628). Prior to any modifications, the sialylglycopeptide obtained from hen egg yolk contains sialic acid $\alpha(2,6)$ linked to an N-glycan chain (structure 1, p. 1628). Sialylglycopeptide (1) can be treated with neuraminidase to give desialylated

structure (2). Subsequent treatment of structure (2) with an α(2,3)-sialyltransferase followed by α(1,3)-fucosyltransferase provides dimeric sialyl Lewis x linked to asparagine (structure 4). Lin *et al.* further showed that dimeric sLe^x is an inhibitor of E-selectin (p. 1625, column 2, last paragraph). E-selectin is a glycoprotein expressed on the surface of activated endothelial cells. The interaction between E-selectin and oligosaccharides present on the surface of neutrophils is an important event in tissue injury, infection and cancer metastasis (p. 1625, introduction).

Bundy *et al.* teaches lectin and carbohydrate affinity capture surfaces for mass spectrometric analysis of microorganisms. The preparation of carbohydrate affinity probes is a two-step process, consisting of first immobilizing streptavidin to the membrane surface, followed by complexing the biotinylated carbohydrates to the immobilized streptavidin (p. 752, column 2). The glycoconjugate-based membrane biocapture surface is then exposed to a microbial sample and the microbial proteins are allowed to bind to the immobilized biotinylated carbohydrates during a 2 h incubation (p. 753, column 1). The bound microbial sample was then lysed and the protein was analyzed by mass spectrometry.

The "Avidin-Agarose" immobilized immunochemical of Calbiochem is an avidin-based matrix for chromatography of biotinylated proteins, peptides and ligands.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Shao *et al.*, concerning a method for characterizing lectin specificity using streptavidin-biotinylglycans, with the teachings of Lin *et al.*, regarding the enzymatic synthesis of a dimeric sialyl Lewis x glycopeptide,

with the teachings of Bundy *et al.*, regarding lectin and carbohydrate affinity capture surfaces for mass spectrometric analysis of microorganisms, with the "Avidin-Agarose" product offered by Calbiochem. One would have been motivated to combine the teachings in order to receive the expected benefit, as suggested by Bundy *et al.*, and exemplified by Calbiochem, that immobilized biotinylglycans can be used to purify and characterize proteins. With respect to characterizing proteins, the immobilized biotinylglycans would be useful for clinical diagnosis, food safety, and biological terrorism since the homogenous biotinylglycans can be used to pull out and identify microorganisms from a complex sample matrix (Bundy *et al.*, p. 751, column 2). With respect to using the immobilized biotinylglycans to purify proteins, a homogenous product of high purity would be obtained, which one of ordinary skill in the art would know and appreciate when the proteins are used for pharmaceutical purposes since it is well-known that impurities can lead to protein instability and deleterious side effects if formulated into a pharmaceutical composition.

Thus, the claimed invention as a whole is *prima facie* obvious over the combined teachings of the prior art.

Section [0002]

Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Shao *et al.* (Anal. Biochem. 1992) as applied to claims 1-2, 11 and 13 above, and further in view of Lin *et al.* (Bioorg. & Med. Chem. 1995) and Fournet *et al.* (Eur. J. Biochem. 1987).

The teachings of Shao *et al.* were as described above in the claim rejections under 35 USC § 102 and the teachings of Lin *et al.* were as described above in section [0001] of the claim rejections under 35 USC § 103. Shao *et al.* and Lin *et al.* do not teach a process for the preparation of FITC-bonded asparagine-linked oligosaacharides of formula (7).

Fournet *et al.* teaches the primary structure of an N-glycosidic carbohydrate unit derived from *Sophora japonica* lectin. To prepare the structure for characterization, the major glycopeptides of the lectin were pronase digested, then derivatized with fluorescein isothiocyanate (FITC), and purified by PAGE (abstract). The procedure for FITC-labeling of the glycopeptides is described in the "experimental procedures" under the subheading "exoglycosidase digestion of glycopeptides" (p. 321-322). Supernatant from the pronase digest is reacted with FITC and incubated for 18 h at 4 °C. The suspension was then centrifuged and purified by Sephadex G-10, followed by preparative polyacrylamide gel electrophoresis. The FITC-labeled glycopeptide was then digested with exoglycosidases and analyzed by methylation analysis and NMR spectroscopy.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Shao *et al.*, concerning a method for characterizing lectin specificity using streptavidin-biotinylglycans, with the teachings of Lin *et al.*, regarding the enzymatic synthesis of a dimeric sialyl Lewis x glycopeptide, with the teachings of Fournet *et al.*, regarding the characterization of an N-glycosidic carbohydrate unit derived from *Sophora japonica* lectin. One of ordinary skill in the art

would be aware of the various groups available, such as a biotin or FITC group, for labeling oligosaccharide structures. There is a plethora of microbial receptors that are known to bind to oligosaccharide substrates. Therefore, if one is to characterize the specificity of these receptors, one of ordinary skill in the art would know that an array of diverse oligosaccharides labeled with a means for detection would be necessary. It would have been *prima facie* obvious to one of ordinary skill in the art to prepare various oligosaccharide structures, using the glycosyltransferase enzymes described by Lin *et al.*, with various labels, as described by Shao *et al.* and Fournet *et al.*, to enable detection of the structure depending on the type of assay and detector used. Moreover, one would have been motivated to combine the teachings in order to receive the expected benefit, as suggested by Shao *et al.*, and exemplified by Fournet *et al.*, that FITC-labeled oligosaccharides permit the direct and immediate detection of the compounds, whereas biotinylated oligosaccharides require secondary binding with either avidin which has high affinity for biotin, or a lectin which binds to the oligosaccharide, conjugated with a visualization marker (such as horseradish peroxidase coupled to the lectin Sambucus nigra as in Shao *et al.*, or alkaline-phosphatase-labeled avidin), prior to detection. A skilled artisan is well aware that the characterization of a protein can result in the identification of inhibitors that are useful in pharmaceutics, such as inhibitors of E-selectin which is involved in tissue metastasis (Lin *et al.*, p. 1625, introduction).

Thus, the claimed invention as a whole is *prima facie* obvious over the combined teachings of the prior art.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SCARLETT GOON whose telephone number is 571-270-5241. The examiner can normally be reached on Mon - Thu 7:00 am - 4 pm and every other Fri 7:00 am - 12 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562 and Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leigh C. Maier/
Primary Examiner, Art Unit 1623
May 9, 2008

/SCARLETT GOON/
Examiner
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